JPPT | National Survey

Survey of Pediatric Pharmacy Residency Program Directors and Former Residents on Post-Graduate Training Paths

Corinne N. Songer, PharmD; Deborah S. Bondi, PharmD; Lauren M. Oliveri, PharmD; Jennie B. Jarrett, PharmD; and Kirsten H. Ohler, PharmD

OBJECTIVE There are currently no data comparing outcomes of traditional vs pediatric-focused PGY1 residency programs. The primary objective of the survey was to identify if a difference in resident preparedness for a PGY2 pediatric pharmacy residency exists between these PGY1 program types.

METHODS This survey-based study included all PGY2 pediatric residency program directors (RPDs) in 2021 and PGY2 pediatric pharmacy residents who completed residency between 2016–2020. Information regarding training paths of residents, such as type of PGY1 completed, and preparedness at the start of a PGY2 pediatric residency was collected. Preparedness for both general and pediatric-specific elements were assessed.

RESULTS A total of 101 respondents were included: 36 RPDs and 65 previous residents. RPDs felt residents who completed a pediatric-focused PGY1 were more prepared in baseline knowledge of pediatric diseases; otherwise, residents were similar across residency types in their perceived preparation for a PGY2. Pediatric-focused PGY1 residents felt significantly more prepared in pediatric baseline knowledge (96% vs 75%, p = 0.002) and managing pediatric emergencies (96% vs 50%, p = 0.002) than those who completed a traditional PGY1 program. There was no difference for patient care or clinical research skills. Residents in both groups obtained pediatric pharmacist jobs and felt equally prepared for transitioning into their first post-residency job.

CONCLUSIONS Despite a difference between the PGY1 resident groups in perceived baseline pediatric knowledge and preparedness to manage pediatric emergencies, similar post-residency jobs were obtained. Respondents felt equally prepared to begin their pediatric careers regardless of the type of PGY1 residency completed.

ABBREVIATIONS PGY1, post-graduate year 1; PGY2, post-graduate year 2; RPD, residency program director

KEYWORDS pediatric pharmacy; postgraduate training; residency; education

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Introduction

Pharmacists can choose to pursue residency training programs to further their education and professional development beyond what is obtained during their Doctor of Pharmacy (PharmD) curriculum. Residency programs are categorized by year of training: postgraduate year one (PGY1) and postgraduate year two (PGY2). The purpose of a PGY1 pharmacy residency is to enhance general pharmacotherapy knowledge and to manage medication-related issues for patients with a variety of disease states beyond entry-level competence.[1,2] A PGY2 is designed to develop expert knowledge, skills and abilities in an advanced area of pharmacy practice, such as pediatrics.[2]

In 2020, there were 1380 PGY1 pharmacy residency programs in the United States offering 3906 PGY1 residency positions.[3] Pharmacy residency programs are highly competitive due to the limited number of positions and increasing number of pharmacy graduates each year.[4] Of the 6200 applicants for PGY1 programs and 1200 applicants for PGY2 programs, only 63% and 73% successfully attained a pharmacy residency in 2020, respectively.[5] Applicants have the additional challenge of screening and identifying programs which best meet their training goals. For those interested in pediatric pharmacy, the decision may be more difficult because of the advent of PGY1 residency programs within children's hospitals. In 2020, 42 (3%) of PGY1 programs were housed in a children's hospital.[3] The

American Society of Health-System Pharmacists (ASHP), the body responsible for residency accreditation, holds all inpatient PGY1 programs, regardless of type of institution, to the same accreditation standards and objectives.[6] ASHP requires each PGY1 resident to achieve competency in 4 specific areas: patient care; advancing practice and improving patient care; leadership and management; and teaching, education, and dissemination of knowledge. While, they do not require specific clinical experiences to achieve these competencies, ASHP does require that no more than one-third of the residency year focuses on a specific disease state or patient population.[7,8] Applicants interested in a career in pediatric pharmacy must then decide which pharmacy residency to pursue: a traditional PGY1 (adult +/− pediatric learning experiences) or a pediatric-focused PGY1 (in a children's hospital or >50% of the year in pediatric learning experiences).[9]

Previous publications have highlighted potential advantages and disadvantages of each type of PGY1 residency.[9,10] Traditional PGY1 programs may include some pediatric experiences but typically focus on adult pharmacotherapy. Pediatric-focused PGY1 programs aim to allow residents to concentrate on their pediatric knowledge at the start of their pharmacy career through access to a wider range of available pediatric rotations and preceptors.[9] Due to increased exposure to pediatric pharmacy, graduates of pediatric-focused PGY1 residencies may transition into PGY2 pediatric pharmacy programs more easily than graduates of traditional PGY1 programs. Conversely, traditional PGY1 programs are proposed to provide a broader understanding of adult practice, which can then be extrapolated to pediatric patients during patient care scenarios where there is a paucity of data regarding the safe use of many medications.[9,10]

There are currently no objective data directly comparing outcomes between the two program types. The aim of this survey-based study was to determine if differences between traditional and pediatric-focused PGY1 training programs influence residents' perceived preparation and success in transitioning into PGY2 pediatric pharmacy programs from the perspective of residents and residency program directors (RPDs).

Methods

Design. This was an observational, cross-sectional, survey-based, cohort study, which included all PGY2 pediatric pharmacy RPDs in 2021 and any pharmacist who completed PGY2 pediatric pharmacy residency training from 2016–2020. Pharmacists who did not complete a PGY2 pediatric pharmacy residency or who graduated from their PGY2 pediatric residency program prior to 2016 were excluded. The study protocol was approved by the Institutional Review Board at the University of Illinois at Chicago. The survey was disseminated using the American College of Clinical Pharmacy Pediatric Practice and Research Network listserv. All active RPDs were also emailed the survey directly using contact information obtained from the ASHP Online Residency Directory in February 2021. The emails were sent simultaneously to both groups on February 1, 2021. The survey was kept open for a period of 2 weeks and email reminders were sent halfway through the survey period and on the last day the survey was open (February 8 and 15, respectively). Each respondent could only complete the survey once.

Survey Tool. Two surveys were developed: 1 designed for RPDs and 1 for past PGY2 pediatric pharmacy residents, which comprised of 42 and 46 questions, respectively. The surveys were developed using Qualtrics online software (Qualtrics Labs Inc, Provo, UT). The question format included multiple-choice and scale-based responses. Some questions allowed multiple responses and free-text comments. Respondents could skip questions, except for the first question, which was designed to establish inclusion criteria for the survey. Question content was developed using the potential advantages and disadvantages of each residency type listed in previous publications.[9,10] The surveys were pilot tested by a group of ten pediatric pharmacists who did not meet the inclusion criteria. The pilot testers consisted of former RPDs and former PGY2 pediatric residents who completed their residencies greater than 5 years ago.

The RPD survey solicited information about their length in practice, previous training, and the training paths of their previous residents. The RPDs were then asked their perceptions of all of their prior residents' preparedness at the start of their PGY2 year for general and pediatric-specific pharmacy practice. The resident survey solicited information regarding their PGY1 training, such as the type and percent of rotations completed in pediatric areas. Residents were also asked to rate their self-reported preparedness entering their PGY2 pediatric pharmacy program for patient care skills, pediatric baseline knowledge, management of pediatric emergencies, and performing clinical research. Information regarding first post-residency job and their self-evaluated preparedness for job-related duties was also assessed. All respondents were additionally asked to provide a free text of their perceived advantages and disadvantages of each type of PGY1 program. Copies of the survey questions are available upon request of the corresponding author.

Outcomes. The primary outcome of the survey was to identify if there was a difference in perceived preparedness for a PGY2 pediatric pharmacy residency between residents who completed a traditional PGY1 program compared with those who completed a pediatric-focused PGY1 program from the perspective of both RPDs and residents. Secondary outcomes were

to evaluate trainees' perceived differences between traditional and pediatric-focused PGY1 training programs and evaluate the type of post-PGY2 position obtained and preparedness for that position based on type of PGY1 completed.

Data Collection and Analysis. Survey results were captured in the Qualtrics online survey. All completed and partially completed surveys were included, using the actual number of respondents for each question in the analysis. Results were analyzed using descriptive statistics. Statistical analysis was performed with SPSS (version 26, IBM Corp, Armonk, NY). An alpha of <0.05 was considered significant for all analyses. Open-ended questions regarding perceptions of the different PGY1 types were analyzed and grouped based on grounded theory methodology.[11,12] Two investigators (CS and KO) identified themes based on the response, which were then validated by a third investigator (DB). Each response was coded for themes, and multiple themes were allowed for each response.

Results

At the time of the survey, the ACCP Pediatric PRN listserve had 448 active, full members. One hundred thirty-one respondents began the survey, of which 30 were excluded due to not being an RPD or PGY2 pediatric resident who graduated in the last 5 years. Of the remaining 101 respondents included in the analysis, 36 were RPDs and 65 were previous residents; 5 of the respondents were included in both groups.

RPD Results. Thirty-six RPDs began the survey, which represents a response rate of 50% (72 RPDs were in the directory in February 2021). Not all participants completed the survey, thus the total number of respondents for each question is reflected in the denominator. The RPD demographics can be found in Table 1. All of the RPDs worked at an institution that accepts pharmacy students for advanced pharmacy practice experiences, 31 (89%) worked in an academic medical center, and 18 (51%) were affiliated with a college of pharmacy. All RPDs had a PGY1 pharmacy residency program also at their institution (22 [65%] traditional PGY1 program vs 12 [35%] pediatric-focused PGY1). RPDs reported they early committed a PGY2 pediatric pharmacy residency position 40% of the time (range 0-100%) over the last 5 years.

When asked about training paths of their previous PGY2 pediatric pharmacy residents, 19 (54%) RPDs reported experience having residents from both traditional and pediatric–focused PGY1 programs. Those 19 RPDs were then asked to compare their perception of residents' preparedness at the start of their PGY2 pediatric residency based on the type of PGY1 completed (Figure 1). Thirteen of 16 RPDs (81%) felt that residents who completed a pediatric-focused PGY1 were more prepared in their baseline knowledge of pediatric disease states. For pediatric medication therapy knowledge, 6 (46%) of the RPDs felt pediatric-focused PGY1s were more prepared, compared with 6 (46%) who felt the residents were similar. Ten (59%) RPDs felt the residents were similar in preparedness for management of pediatric emergencies, while the remainder felt pediatric-focused PGY1s were more prepared. Overall, the RPDs felt that resident preparedness was similar between the two groups for collection of relevant patient information, development of a medication plan, interaction with the medical team, management of transitions of care, and time management skills.

All RPDs were asked their perceived advantages and disadvantages of each type of PGY1 program. The reported themes are listed in Table 2. The most frequent responses for each category were related to exposure to and knowledge of pediatric vs adult patient care experiences.

Resident Results. Sixty-five past pediatric PGY2 residents started the survey, of which 26 (40%) completed a pediatric-focused PGY1 program and 39 (60%) completed a traditional PGY1. Resident demographics can be found in Table 3.

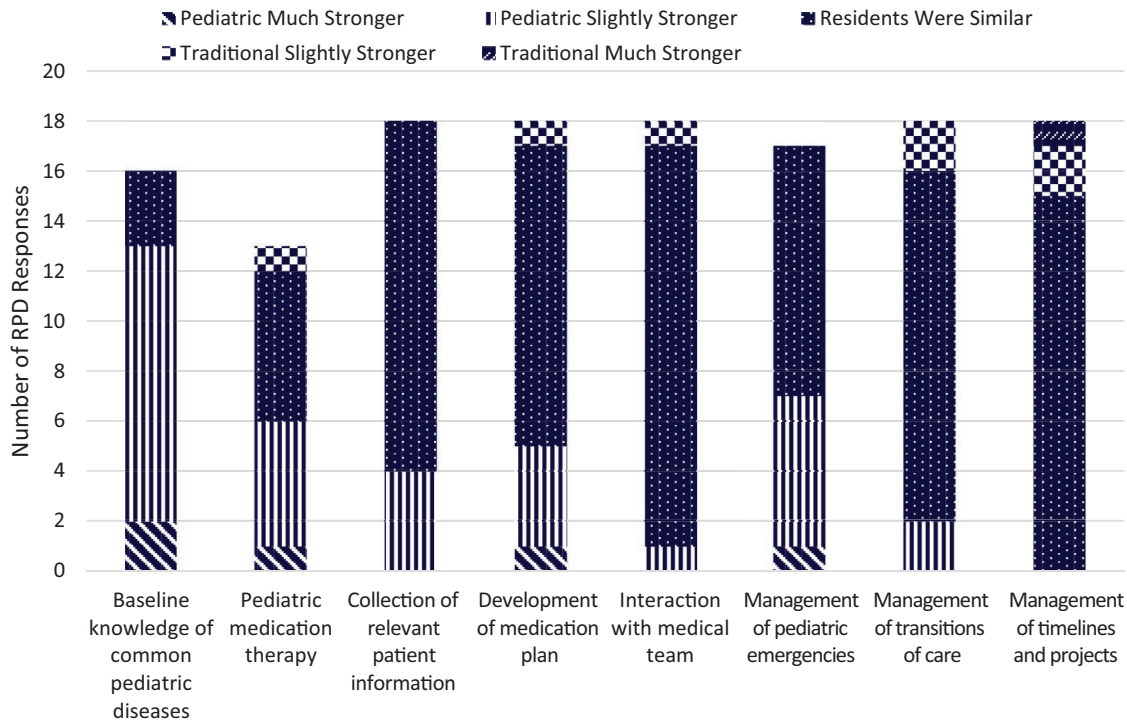
Residents who completed a pediatric-focused PGY1 were able to complete a significantly higher percentage of their PGY1 rotations in pediatric areas (98.4% ± 3.6 vs 22.9% ± 11.3, $p < 0.01$). Pediatric-focused PGY1 residents were more likely to have pediatric research opportunities available to them during their PGY1

Table 1. Baseline Characteristics of Residency Program Directors (RPDs)

Characteristic	RPDs (N = 36)
Length in practice (years); median (range)	11 (4–35)
Length as RPD (years); median (range)	3 (0.5–15)
Board certified; n (%)	35 (97)
Completed PGY1; n (%) Traditional Pediatric	32 (89) 25 (78) 6 (19)
Completed Pediatric PGY2; n (%)	22 (61)
Type of Pediatric Institution Currently; n (%) Free-standing children's hospital Free-standing children's hospital within a larger health system Children's hospital within an adult institution Pediatric floor/unit within an adult institution	 10 (29) 8 (23) 16 (46) 1 (2)

PGY1, post-graduate year 1; PGY2, post-graduate year 2

Figure 1. Perception of resident performance at the start of their PGY2 pediatric pharmacy residency by RPDs who previously had both traditional and pediatric-focused trained PGY2s (N = 19).



PGY1, post-graduate year 1; PGY2, post-graduate year 2; RPD, residency program director

Table 2. Residency Program Directors Perceived Advantages and Disadvantages of Each PGY1 Residency Type

PGY1 Residency Type	Advantages (n)	Disadvantages (n)
Pediatric-Focused	Increased pediatric knowledge (17) Increased pediatric exposure or experience (15) Ability to specialize earlier in career (5) None (3) Ability to obtain a job without a PGY2 (2) Increased mentoring (1)	Limited adult exposure/experience (13) Limited adult knowledge (10) Limited applicability of adult medicine to adult-sized patients (9) None (3) Narrow-focused (2) Little incentive to do a PGY2 (2) Develops a false sense of confidence (1) Residents are more passive (1) Lack of autonomy during PGY2 (1)
Traditional	Increased adult exposure or experience (18) Increased/broader knowledge (14) Applicability of adult knowledge to pediatric patients (14) Development of general pharmacy skills (6) Well-rounded (5) Ensure commitment to pediatrics as career (4) Increased research experience (2)	Limited pediatric experience/exposure (16) Limited pediatric knowledge (10) None (6) Steeper learning curve during PGY2 (5) Delayed specialization in pediatrics (4)

PGY1, post-graduate year 1; PGY2, post-graduate year 2

Table 3. Baseline Characteristics and Pediatric Experiences During PGY1 Programs

Characteristic	Pediatric-Focused (N = 26)	Traditional (N = 39)	p value
Years post-residency; mean (SD)	2.1 (1.4)	2.9 (1.4)	0.04
Board certified; n (%)	15 (68)	22 (69)	0.69
Type of pediatric institution for PGY1; n (%)			
Free-standing children's hospital	16 (62)	0 (0)	
Free-standing children's hospital within a larger health system	10 (38)	4 (10)	
Children's hospital within an adult institution	0 (0)	23 (59)	
Pediatric floor/unit within an adult institution	0 (0)	12 (31)	

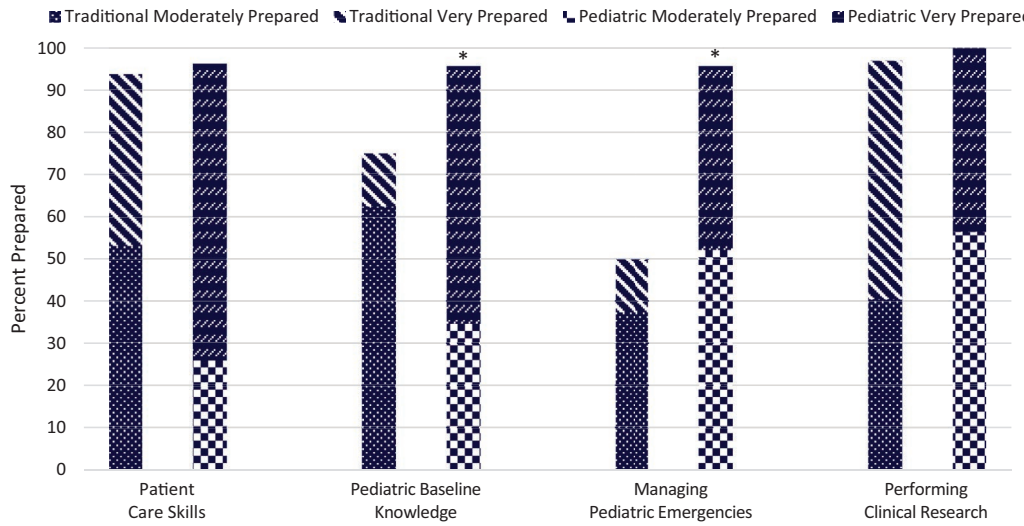
PGY1, post-graduate year 1

(24 [100%] vs 29 [76%], p = 0.01). The opportunity to complete a pediatric presentation, defined as a continuing education presentation, journal club, or other large presentation, was similar between the two groups (24 [100%] vs 33 [87%], p = 0.15). Those who completed a pediatric research project or presentation were not significantly different between the groups (24 [100%] vs 27 [93%], p = 0.5 and 23 [96%] vs 33 [100%], p = 0.42, respectively). Eighteen (78%) pediatric-focused PGY1 trained residents stated there was a PGY2 pediatric pharmacy residency at the same institution compared with 13 (41%) in the traditional PGY1 group (p=0.01). While there was a higher percentage of PGY2 pediatric pharmacy residency programs at institutions with a pediatric-focused PGY1, the opportunity to early commit to that program was significantly lower (10 [56%] vs 12 [92%], p = 0.03). Among those with the opportunity to early commit, the early commitment rate was not different between the groups (6 [60%] vs 9 [75%], p = 0.45).

Residents reported their perceived preparedness at the start of their PGY2 program (Figure 2). Those who completed a pediatric-focused PGY1 were more likely to report they felt prepared in their pediatric baseline knowledge (22 [96%] vs 24 [75%], p = 0.002) and managing pediatric emergencies (22 [96%] vs 16 [50%], p = 0.002) compared with those who completed a traditional PGY1 program. Preparation in their patient care skills and performing clinical research were similar between the groups.

Each resident was asked their rationale for completing their specific PGY1 type and the responses were coded for themes. The responses are listed in Table 4. Past residents were also asked their perceived advantages and disadvantages of each type of PGY1 program.

Figure 2. Residents' self-reported preparedness at the start of pediatric PGY2.



PGY2, post-graduate year 2

*p = 0.002

Table 4. Residents' Rationale for Completing Each PGY1 Residency Type

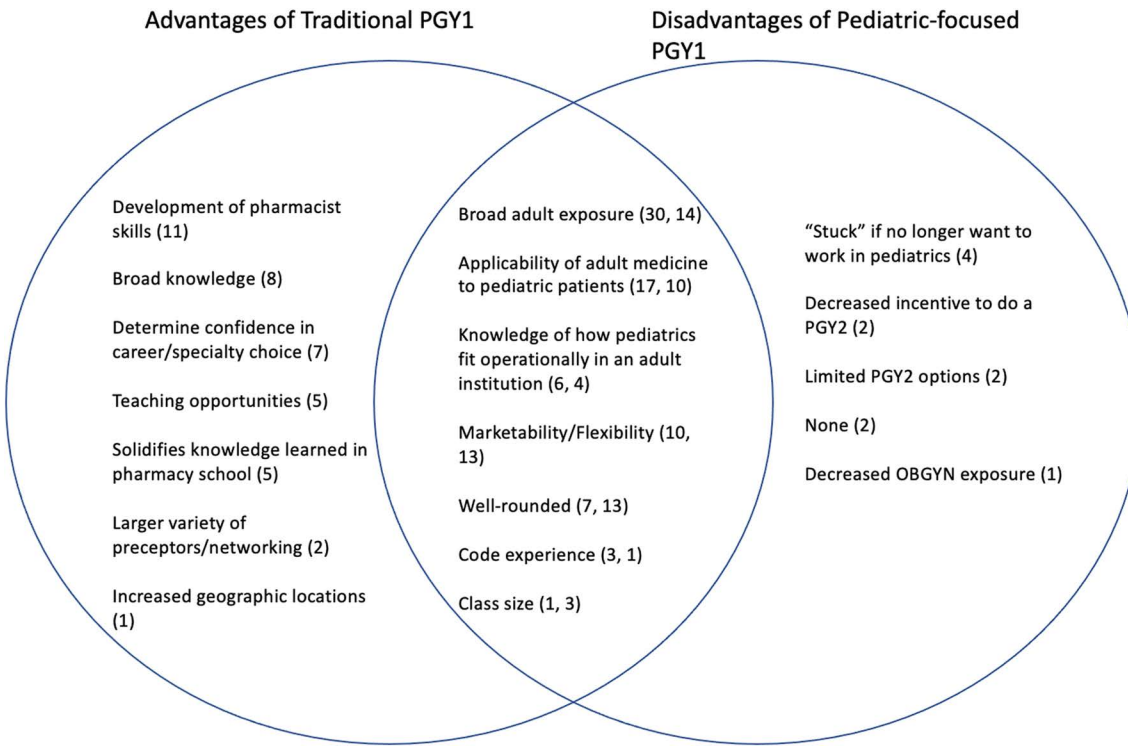
PGY1 Residency Type	Rationale (n)
Pediatric-Focused	Confident in pediatrics as specialty (16) No interest in adult medicine (7) Ability to subspecialize in PGY2 (6) Increased pediatric knowledge (3) Ability to obtain a job without a PGY2 (2) Increased chance of obtaining a PGY2 (1) Specific institution of interest (1)
Traditional	Broad experience/exposure (17) Hope to become more well-rounded (12) Explore other interests/confirm pediatrics as specialty of choice (12) Build foundational knowledge (10) Build upon general pharmacist skills (8) Ability to work in an academic medical center (4) Matched into the program (1)

PGY1, post-graduate year 1; PGY2, post-graduate year 2

The themes reported from the residents are listed in Figures 3 and 4. The perceived advantages of one program type often overlapped with the perceived disadvantages of the other program type.

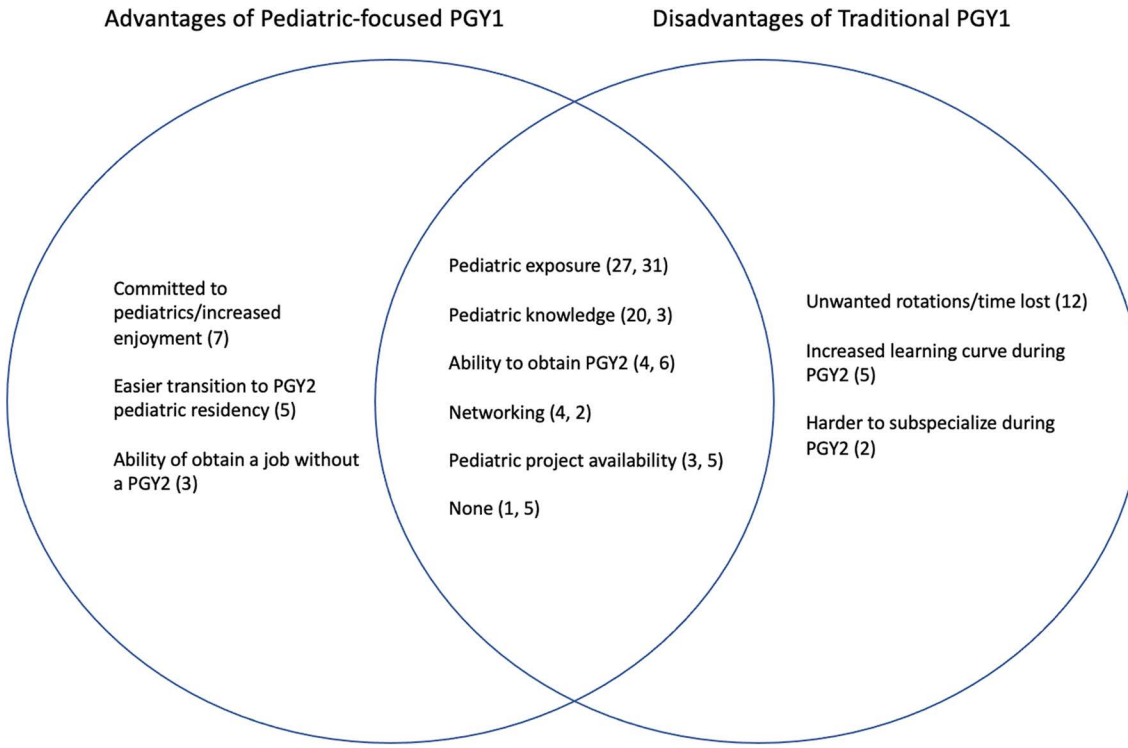
Residents reported characteristics of their first job post-residency. The majority of residents from both the pediatric-focused PGY1 and traditional PGY1 groups obtained a pediatric pharmacist position (22 [100%] vs 30 [94%], p = 0.51), with 2 residents in the traditional PGY1 group obtaining a faculty position. Residents who completed a pediatric-focused PGY1 were more likely to obtain a post-PGY2 position at a free-standing children's hospital than those who completed a traditional PGY1 (17 [74%] vs 13 [41%], p = 0.01). Job responsibilities between groups were also similar for patient care (22 [100%] vs 30 [94%], p = 1), operational/dispensing duties (8 [36%] vs 17 [53%], p = 0.23), emergency response (15 [68%] vs 25 [78%], p = 0.41), clinical research (11 [50%] vs 17 [53%], p = 0.82), precepting (21 [96%] vs 30 [94%], p = 0.79) and didactic teaching (8 [36%] vs 17 [53%], p = 0.23) between pediatric-focused and traditional PGY1s, respectively. Preparedness entering their first post-PGY2 position for their clinical duties was also assessed between the two groups (Figure 5). Residents

Figure 3. Residents' perceived advantages of traditional PGY1 residencies and disadvantages of pediatric-focused PGY1 residencies. (N-values for advantages are listed first in the center circle.)



PGY1, post-graduate year 1; PGY2, post-graduate year 2

Figure 4. Residents' perceived advantages of pediatric-focused PGY1 residencies and disadvantages of traditional PGY1 residencies. (N-values for advantages are listed first in the center circle.)



PGY1, post-graduate year 1; PGY2, post-graduate year 2

in both groups felt prepared transitioning into their first post-PGY2 position (22 [100%] vs 32 [100%], p = 1).

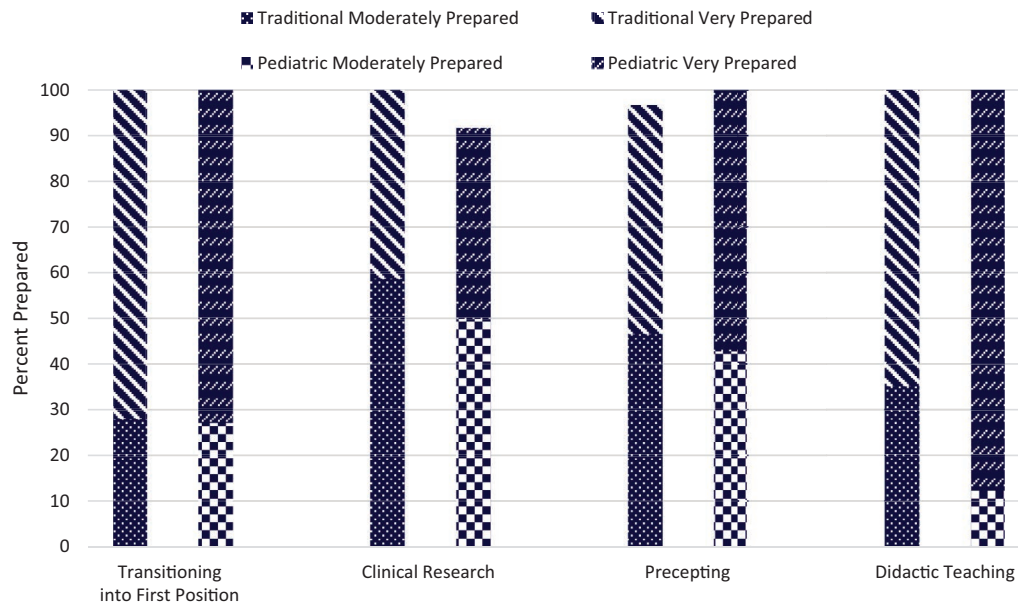
Discussion

Applicants for pharmacy residency programs have difficult decisions to make when choosing which program would best meet their career and training goals. For those who have an interest in pediatrics, they have the additional decision of type of PGY1 residency to pursue: traditional vs pediatric-focused. Often, mentors can heavily influence the residency paths students choose based on their own perceptions of the ideal residency path for students. This is the first survey, to our knowledge, to assess preparedness for a PGY2 pediatric pharmacy residency based on the type of PGY1 program completed and provides objective data about the differences in PGY1 programs for those interested in a pediatric pharmacy career.

Results of our survey suggest that residents who complete a pediatric-focused PGY1 program are subjectively more prepared to enter a PGY2 pediatric pharmacy residency with regards to baseline knowledge of pediatric disease states. These results are to be expected, as residents in pediatric-focused PGY1 programs are exposed to pediatric patients for a higher percentage of their PGY1 year compared with those who complete a traditional PGY1 program. However, many of the RPDs who completed the survey felt that the differences in baseline pediatric knowledge could be overcome throughout the PGY2 year and thus, did not affect overall resident performance.

In a commentary by Shaddix et al.,[9] the highlighted advantages and disadvantages of each type of PGY1 program were similar to some of our survey results. The primary proposed advantage of a pediatric-focused PGY1 was increased pediatric exposure and increased availability of pediatric projects. Despite potential differences in pediatric exposure during their PGY1, the majority of RPDs felt that residents were similarly prepared for pediatric emergencies, perhaps suggesting that while PGY2 resident comfort level may be increased with a pediatric-focused PGY1, the actual performance of the residents when assessed by preceptors may be similar. While our survey found a difference in the availability of pediatric research projects favoring pediatric-focused PGY1 programs, those PGY1 residents who wanted to perform pediatric research were able to do so regardless of program type.

Figure 5. Residents' self-reported preparedness for their first post-residency job.



Our survey results suggest the type of PGY1 program completed did not affect the type of first post-residency job obtained or preparedness for that job. All residents felt equally prepared to transition into their first post-PGY2 residency position and perform the duties associated with that position. All clinical pharmacy positions obtained were within pediatric pharmacy. This suggests that regardless of variations in subjective preparedness when entering a PGY2 pediatric pharmacy residency, residents from both types of PGY1 programs graduate from their PGY2 programs with the same subjective confidence and skills to enter their first post-PGY2 position, which may be the more important long-term outcome. Interestingly, both individuals who entered a faculty position post-PGY2 residency completed a traditional PGY1 residency. Prior commentary has noted that a higher proportion of traditional PGY1 programs have a primary affiliation with a college of pharmacy, which may attract candidates who are interested in academia.[10]

Survey respondents noted that there was an increased learning curve when starting a PGY2 pediatric residency for those who completed a traditional PGY1 residency; however, we did not assess the difference in the learning curve for students transitioning into a pediatric-focused PGY1 compared with a traditional PGY1 program, which may have provided additional insight for students when researching PGY1 programs. Several survey respondents noted that a portion of the information learned during a traditional PGY1 residency is not applicable to practice as a pediatric pharmacist, considering many rotations "uninteresting" or "wasted time." While pediatric pharmacists may not use all of the information learned during a traditional PGY1, many of the general skills developed, such as evidence-based medicine and critical thinking, can be applied to pediatric pharmacy. Additionally, data from adult practice is often extrapolated to pediatrics as investigation of newer therapies in this population often lags behind studies in adult patients. Preceptors and mentors can aid their residents in applying their broader knowledge base and skill set to pediatric patients, further refining these skills in a different patient population. Another potential benefit of obtaining a broader knowledge base and skill set is seen in the respondents' perceived increased flexibility when pursuing jobs and increased comfort when caring for adult-sized pediatric patients.

A perceived disadvantage of traditional PGY1 programs is the limited opportunity to early commit to a PGY2 pediatric residency. Initially, this seems to be supported as only 41% of respondents in the traditional PGY1 group reported having a PGY2 pediatric residency at the same institution as their PGY1. However, the ASHP residency directory shows 72% of PGY2 pediatric programs are at institutions with a traditional PGY1 program, suggesting we may not have reached a representative population of responders.[3] Additionally, we found that among the residents surveyed with the opportunity to early commit, the actual early commitment rate was not different between the groups (6 [60%] vs 9 [75%], $p = 0.45$). Thus, the perceived disadvantage of limited early commitment opportunities with a traditional PGY1 program may not be a barrier depending on the PGY1 programs to which the candidates apply.

Our study is not without limitations. First, the limited number of survey responses may reduce the external

validity of the survey. The overall response rate for residents cannot be calculated since the total number of Pediatrics PRN members who met inclusion criteria is unknown. We can estimate the response rate was low. Based on the ASHP match results from 2015–2019 (correlating to graduations in 2016–2020), there are up to 346 pharmacists who could have completed a PGY2 pediatric pharmacy residency. This means that our survey of 65 former residents may represent as little as 19% of the potential group. Respondents were also allowed to skip questions and could have avoided answering questions that were longer or confusing. Conversely, respondents could have only answered questions about which they felt strongly. These could have skewed the data set presented. There is also potential for selection bias due to the use of electronic mail list serves as the survey dissemination tool because it is not likely that our entire intended former resident population received the survey invitation. It is likely that our survey had recall bias within the results. Residents were asked to recall their thoughts and preparedness from as long as five years ago and RPDs were asked to recall their residents throughout their careers, which may be skewed depending on how long they have been in practice. We did not collect whether respondents obtained their first position post-PGY2 residency at the same institution at which they trained. While both groups reported a similar level of preparedness for their first post-PGY2 position, the implications this information may have on these findings is unknown. There is also a potential RPD bias based on their training and experiences, further skewing the data. Given the small number of responding RPDs who completed a pediatric PGY1, a comparison of responses based on RPD training was not conducted. Lastly, our survey could not account for inherent differences in pediatric exposure between PGY1 programs, such as patient population or the pediatric pharmacist's role at that institution. Despite these potential limitations, our survey results provide information where a previous gap in knowledge existed.

Conclusions

Despite perceived differences in baseline knowledge of pediatric disease states and preparedness to manage pediatric emergencies, residents who completed either PGY1 residency type obtained similar post-PGY2 jobs and felt equally prepared to begin those jobs, suggesting that any perceived differences at the start of the year were likely overcome as the year progressed. Multiple advantages and disadvantages to both types of PGY1 programs were highlighted by RPDs and previous PGY2 pediatric pharmacy residents. Residency candidates should consider their training and long-term career goals when applying this data to determine their ideal PGY1 program. Mentors who are providing advice to trainees should highlight both advantages and disadvantages of each type of PGY1 residency to broaden the perspective of potential residency candidates as they choose the PGY1 program that best suits their needs.

Article Information

Affiliations. Department of Pharmacy (CNS), Ascension St. John Hospital, Detroit, MI; Department of Pharmacy Practice (LMO, JBJ, KHO), College of Pharmacy, University of Illinois at Chicago, Chicago, IL; Children's Hospital University of Illinois (LMO, KHO), University of Illinois Hospital & Health Sciences System, Chicago, IL; Department of Pharmacy (DSB), University of Chicago Medicine Comer Children's Hospital, Chicago, IL.

Correspondence. Corinne N Songer, PharmD; corinne.songer@ascension.org

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Ethical Approval and Informed Consent. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation and have been approved by the appropriate committees at our institution. However, given the nature of this study, informed consent was not required by our institution.

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